

Amendment and Reply dated April 19, 2005 for X16699_US
09/748,739 - Lockridge & Watkins

Remarks

Numerous typographical, grammatical, and publishing errors were found in the published application, US 2002/0119489 A1. The "Amendments to the Specification," shown on pages 2-19 of this response, is a list of errors falling within these categories. No new matter has been added to this application by this amendment.

The Applicants appreciate the Examiner's straightforward comments regarding claim amendments and have amended the claims accordingly. The Examiner has rejected Claims 1 and 2 under 35 USC § 112, second paragraph, as being indefinite because no Tryptophan exists at position 328 of SEQ ID NO:2. As noted by the Examiner, SEQ ID NO:2 includes a 28 amino acid signal sequence such that, in SEQ ID NO:2, the Tryptophan to which the Applicants refer is located at amino acid position 356. Claim 1, and thus its dependent Claim 2, has been amended to change "position 328" to "position 356."

The Examiner has objected to Claim 1 because Tryptophan was misspelled ("Tryptophane"). The spelling of Tryptophan in this claim and throughout the specification has been corrected through this amendment.

The Examiner has rejected Claims 1 and 2 under 35 USC § 112, first paragraph, as failing to comply with the written description requirement because of new matter. In particular, the Examiner rejected the use of the word "about" when describing the beginning of the mature protein in SEQ ID NO:2. The Examiner also rejected the use of the word "about" under 35 USC § 112, second paragraph, as being indefinite. In view of these rejections, the Applicants have amended Claim 1, and thus dependent Claim 2, by deleting the word "about."

Additionally, the Examiner has rejected Claim 2 under 35 USC § 112, second paragraph, as being indefinite, stating that it fails to indicate what is being compared to the butyrylcholinesterase variant. Claim 2 has been amended such that it is consistent with the specification, reciting that the butyrylcholinesterase variant is "compared to human butyrylcholinesterase."

Finally, the Examiner has provisionally rejected Claims 1 and 2 under obviousness-type double patenting over Claims 1 and 8 of copending Application 10/413,432. The

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Applicants have amended Claim 1, and thus its dependent Claim 2, such that it comprises the amino acid sequence of SEQ ID NO:2. The Examiner states that SEQ ID NO:52 of the '432 Application has "100% seq id to amino acids 29-602 of seq. Id. 2" of the instant application and "possesses a trp at position 328." The Applicants respectfully provide herein a comparison of the two sequences:

<u>Met</u>	<u>Asp</u>	<u>Ser</u>	<u>Lys</u>	<u>Val</u>	<u>Thr</u>	<u>Ile</u>	<u>Ile</u>	<u>Cys</u>	<u>Ile</u>	<u>Arg</u>	<u>Phe</u>	<u>Leu</u>	<u>Phe</u>	<u>Trp</u>	<u>Phe</u>	<u>Leu</u>	
-28																	-12
<u>Leu</u>	<u>Leu</u>	<u>Cys</u>	<u>Met</u>	<u>Leu</u>	<u>Ile</u>	<u>Gly</u>	<u>Lys</u>	<u>Ser</u>	<u>His</u>	<u>Thr</u>	<u>Glu</u>	<u>Asp</u>	<u>Asp</u>	<u>Ile</u>	<u>Ile</u>	<u>Ile</u>	
										-1	1						6
Ala	Thr	Lys	Asn	Gly	Lys	Val	Arg	Gly	Met	Asn	Leu	Thr	Val	Phe	Gly	Gly	23
Thr	Val	Thr	Ala	Phe	Leu	Gly	Ile	Pro	Tyr	Ala	Gln	Pro	Pro	Leu	Gly	Arg	40
Leu	Arg	Phe	Lys	Lys	Pro	Gln	Ser	Leu	Thr	Lys	Trp	Ser	Asp	Ile	Trp	Asn	57
Ala	Thr	Lys	Tyr	Ala	Asn	Ser	Cys	Cys	Gln	Asn	Ile	Asp	Gln	Ser	Phe	Pro	74
Gly	Phe	His	Gly	Ser	Glu	Met	Trp	Asn	Pro	Asn	Thr	Asp	Leu	Ser	Glu	Asp	91
Cys	Leu	Tyr	Leu	Asn	Val	Trp	Ile	Pro	Ala	Pro	Lys	Pro	Lys	Asn	Ala	Thr	108
Val	Leu	Ile	Trp	Ile	Tyr	Gly	Gly	Gly	Phe	Gln	Thr	Gly	Thr	Ser	Ser	Leu	125
His	Val	Tyr	Asp	Gly	Lys	Phe	Leu	Ala	Arg	Val	Glu	Arg	Val	Ile	Val	Val	142
Ser	Met	Asn	Tyr	Arg	Val	Gly	Ala	Leu	Gly	Phe	Leu	Ala	Leu	Pro	Gly	Asn	159
Pro	Glu	Ala	Pro	Gly	Asn	Met	Gly	Leu	Phe	Asp	Gln	Gln	Leu	Ala	Leu	Gln	176
Trp	Val	Gln	Lys	Asn	Ile	Ala	Ala	Phe	Gly	Gly	Asn	Pro	Lys	Ser	Val	Thr	193
Leu	Phe	Gly	Glu	Ser	Ala	Gly	Ala	Ala	Ser	Val	Ser	Leu	His	Leu	Leu	Ser	210
Pro	Gly	Ser	His	Ser	Leu	Phe	Thr	Arg	Ala	Ile	Leu	Gln	Ser	Gly	Ser	Ala	227
<u>Phe</u>	<u>Asn</u>	<u>Ala</u>	<u>Pro</u>	<u>Trp</u>	<u>Ala</u>	<u>Val</u>	<u>Thr</u>	<u>Ser</u>	<u>Leu</u>	<u>Tyr</u>	<u>Glu</u>	<u>Ala</u>	<u>Arg</u>	<u>Asn</u>	<u>Arg</u>	<u>Thr</u>	243
<u>227</u>																	
Leu	Asn	Leu	Ala	Lys	Leu	Thr	Gly	Cys	Ser	Arg	Glu	Asn	Glu	Thr	Glu	Ile	260
Ile	Lys	Cys	Leu	Arg	Asn	Lys	Asp	Pro	Gln	Glu	Ile	Leu	Leu	Asn	Glu	Ala	277
Phe	Val	Val	Pro	Tyr	Gly	Thr	Pro	Leu	<u>Gly</u>	<u>Ser</u>	Val	Asn	Phe	Gly	Pro	Thr	293
										287							
Val	Asp	Gly	Asp	Phe	Leu	Thr	Asp	Met	Pro	Asp	Ile	Leu	Leu	Glu	Leu	Gly	310
Gln	Phe	Lys	Lys	Thr	Gln	Ile	Leu	Val	Gly	Val	Asn	Lys	Asp	Glu	Gly	Thr	327

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Trp Phe Leu Val Met Tyr Gly Ala Pro Gly Phe Ser Lys Asp Asn Asn Ser
332
Ile Ile Thr Arg Lys Glu Phe Gln Glu Gly Leu Lys Ile Phe Phe Pro Gly
360
Val Ser Glu Phe Gly Lys Glu Ser Ile Leu Phe His Tyr Thr Asp Trp Val
377
Asp Asp Gln Arg Pro Glu Asn Tyr Arg Glu Ala Leu Gly Asp Val Val Gly
394
Asp Tyr Asn Phe Ile Cys Pro Ala Leu Glu Phe Thr Lys Lys Phe Ser Glu
411
Trp Gly Asn Asn Ala Phe Phe Tyr Tyr Phe Glu His Arg Ser Ser Lys Leu
428
Pro Trp Pro Glu Trp Met Gly Val Met His Gly Tyr Glu Ile Glu Phe Val
445
Phe Gly Leu Pro Leu Glu Arg Arg Asp Asn Tyr Thr Lys Ala Glu Glu Ile
462
Leu Ser Arg Ser Ile Val Lys Arg Trp Ala Asn Phe Ala Lys Tyr Gly Asn
479
Pro Asn Glu Thr Gln Asn Asn Ser Thr Ser Trp Pro Val Phe Lys Ser Thr
496
Glu Gln Lys Tyr Leu Thr Leu Asn Thr Glu Ser Thr Arg Ile Met Thr Lys
513
Leu Arg Ala Gln Gln Cys Arg Phe Trp Thr Ser Phe Phe Pro Lys Val Leu
530
Glu Met Thr Gly Asn Ile Asp Glu Ala Glu Trp Glu Trp Lys Ala Gly Phe
547
His Arg Trp Asn Asn Tyr Met Met Asp Trp Lys Asn Gln Phe Asn Asp Tyr
564
Thr Ser Lys Lys Glu Ser Cys Val Gly Leu
574

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The underlined amino acids are amino acids that occur in SEQ ID NO:2 of the instant application; these include the signal sequence (amino acids -28 to -1) and three additional variants (Phe at position 227, Ser at position 287, and Tyr at position 332). The three lined-through amino acids (Ala at position 227, Gly at position 287, and Met at position 332) are amino acids that occur in SEQ ID NO:52 of the '432 Application, but are different amino acids in SEQ ID NO:2 (see above). Thus, the Applicants assert that SEQ ID NO:2 of the instant application and SEQ ID NO:52 of the '432 Application do not share 100% sequence identity from amino acids 29-602 (or 1-574, as shown above). Applicants further assert that this application, as currently amended, does not conflict with copending Application 10/413,432 as obviousness-type double patenting.

In view of the remarks and amendments provided herein, the Applicants respectfully submit that all rejections and objections have been overcome. The Applicants respectfully

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request entry of the amendments, consideration of the arguments, and withdrawal of all rejections and objections.

The Applicants urge the Examiner to call the Applicants' agent at (317) 433-3422 if a telephone conversation or office interview would be helpful in expediting the prosecution of this case.

Respectfully submitted,

Paula K. Davis

Paula K. Davis
Attorney for Applicants
Registration No. 47,517
Phone: 317-433-3422

Eli Lilly and Company
Patent Division
P.O. Box 6288
Indianapolis, Indiana 46206-6288

April 19, 2005